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EXAMINER	
LEAVITT, MARIA GOMEZ	
ART UNIT	**PAPER NUMBER**
1633	

DATE MAILED: 11/28/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/025,282	BLEYER ET AL.	
	Examiner	Art Unit	
	Maria Leavitt	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *36-60* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *36-60* is/are rejected.

7)☒ Claim(s) *45* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Detailed Action

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on September 30, 2005, has been entered. Species restriction remains correct and active for the request for continued examination of the instant Application..

Claims 36-60 have been amended, and claim 61 has been cancelled by the amendment submitted along with the Request for Continuous Examination filed on September 30, 2005. All new claims are readable on the elected species

Claims 36-60 are pending to which the following grounds of rejection are applicable.

Claims objection

Claim 45 reads, "radopaque"" instead of "radiopaque". Applicant correction is requested.

Claim Rejections - 35 USC § 112 – written description

Claim 54-60 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to any person skilled in the art to which it pertains, or with which it is most nearly connected, at the time the application was filed, that the inventor, at the time the application was filed, had possession of the claimed invention.

Claims 54-60, when given the broadest reasonable interpretation encompass a genus of unspecified radiopaque, implantable biomaterial device comprising a bioabsorbable collagenous

biomaterial including multiple collagenous layer segments that are bonded to one another. The specification describes that it is possible to shape large surface area constructs by combining two or more tela submucosa segments (p. 21, lines 11-13). Additionally, it discloses the use of collagenous biomaterial 10 as and individual layer or multi-layer (p.9, paragraph 2).

To satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail such that the Artisan can reasonably conclude that the inventor(s) had possession of the claimed invention. Such possession may be demonstrated by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and/or formulae that fully set forth the claimed invention. Possession may be shown by an actual reduction to practice, showing that the invention was "ready for patenting", or by describing distinguishing identifying characteristics sufficient to show that Applicant was in possession of the claimed invention (January 5, 2001 Fed. Reg., Vol. 66, No. 4, pp. 1099-11). Moreover, MPEP 2163 states:

> [A] biomolecule sequence described only by a functional characteristic, without any known or disclosed correlation between that function and the structure of the sequence, normally is not a sufficient identifying characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence.

Overall, what these statements indicate is that the Applicant must provide adequate description of such core structure and function related to that core structure such that the Artisan could determine the desired effect. Hence, the analysis below demonstrates that Applicant has not determined the core structure for full scope of the claimed genera.

In analyzing whether the written description requirement is met for genus claims, it is first determined whether a representative number of species have been described by their complete structure. In the instant case, Applicant, provides only one example wherein a plurality of tela submucosa strips can be fused to one another, by compressing overlapping area of the strips under dehydrating conditions, to form an overall planar constructs having a surface area greater than that of any one planar surface of the individual strips used to shape the construct. Additionally, a radiopaque powder can be disposed within these strips (p.21, paragraph 2). Applicant anticipates that collagenous biomaterial 10 (e.g., submucosa layer) can be used as an individual layer or a multilayer. Further, Applicant discloses that shapes can be made by using sutures, staples, and biocompatible adhesives such as collagen binding paste or dehydrating overlapping structures. However, no other specific teachings on a number of other species of a of bioabsorbable collagenous material that are bonded to one another are disclosed other that the submucosa layer comprised in biomaterial 10. Moreover, the specification does not provide any disclosure as to what would have been the required structure for the bonded collagen-based material, or any methods to bind collagenous layers segments to one another.

Applicant, for example, teaches in Fig.1 a cross section of small intestine with the collagenous biomaterial 10 containing a multilayered device, comprising the following layers: tunica submucosa 46, lamina muscularis mucosa 47, from where the tela submucosa can be further delaminated. However, Applicant only states that the collagenous biomaterial 10 can be an individual layer or a multilayer, without any further directions about how these multi-layers can be bonded to one another.

Next then, it is determined whether a representative number of species have been sufficiently described by other relevant identifying characteristics (i.e., to provide a bond to adhere firmly), specific features and functional attributes that would distinguish different members of the claimed genus. In the instant case, no other characteristic in addition to the anticipated statement discussed above is disclosed. Such functional characteristics, however, do not allow one of skill in the art to distinguish the different members of the genera form each other.

Applicant's attention is directed to *In re Shokal*, 113 USPQ 283 (CCPA 1957), wherein it is stated:

> It appears to be well settled that a single species can rarely, if ever, afford sufficient support for a generic claim. *In re Soll*, 25 CCPA (Patents) 1309, 97 F2d 623, 38 USPQ 189; *In re Wahlforss*, 28 CCPA (Patents) 867, 117 F2d 270, 48 USPQ 397. The decisions do not however fix any definite number of species which will establish completion of a generic invention and it seems evident therefrom that such number will vary, depending on the circumstances of particular cases. Thus, in the case of small genus such as the halogens, consisting of four species, a reduction to practice of three, perhaps even two, might serve to complete the generic invention, while in the case of a genus comprising hundreds of species, a considerably larger number of reductions to practice would probably be necessary.

In conclusion, this limited information is not deemed sufficient to reasonably convey to one skilled in the art that Applicant is in possession of any radiopaque, implantable biomedical device, comprising a bioabsorbable collagenous biomaterial including multiple collagenous layer segments that are bonded to one another to promote remodeling of tissue of the patient at a site at which said collagenous biomaterial is implanted, at the time the application was filed. Thus it is concluded that the written description requirement is not satisfied for the claimed genus.

Claim Rejections - 35 USC § 112 - enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 54-60 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 54-60 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for:

An implantable medical device, comprising:

A multi-strip bioabsorbable collagenous based submucosa, wherein a radiopaque marker is disposed in between collagenous layer segments of said multi-strip bioabsorbable collagenous based submucosa to promote remodeling of tissue of the patient at a site at which said bioabsorbable collagenous based submucosa is implanted

does not reasonably provide enablement for a bioabsorbable collagenous biomaterial including multiple collagenous layer segments that are bonded to one another, said bioabsorbable collagenous biomaterial effective to promote remodeling of tissue of the patient at a site at which said collagenous biomaterial is implanted; and a radiopaque marker disposed in between collagenous layer segments of said bioabsorbable collagenous biomaterial.

Claims 54-60 are drawn to a radiopaque, implantable biomaterial device comprising a bioabsorbable collagenous biomaterial including multiple collagenous layer segments that are bonded to one another to promote remodeling of tissue of the patient at a site at which said collagenous biomaterial is implanted. The specification specifically discloses in Fig.1 a cross section of small intestine with the collagenous biomaterial 10 containg a multilayered device, comprising the following layers: tunica submucosa 46, lamina muscularis mucosa 47, from where the tela submucosa can be further delaminated. Additionally, the specification teaches that the collagenous material is radiopaque and can take any shape. Further, Applicant discloses that shapes can be made by using sutures, staples, and biocompatible adhesives such as collagen binding paste or dehydrating overlapping structures (p. 21, lines 16-24). However, Applicant only states that the collagenous biomaterial 10 can be used as an individual layer or a multilayer (p. 9, lines 24-25), without any further directions about how these multi-layers can be bonded to one another. Regarding the teachings of the specification, the specification appears to contemplate a number of strips or layers of submucosa, within which a radiopaque powder can be disposed, however, no other specific teachings of any number of other species of a bonded multilayer of bioabsorbable collagenous material is taught. Claims 54-60 when given the broadest reasonable interpretation encompass a genus of unspecified variants of an unspecified radiopaque, implantable biomaterial device comprising a bioabsorbable collagenous biomaterial including multiple collagenous layer segments that are bonded to one another by any method. The disclosure provided by the Applicant, in view of the prior Art, must encompass a wide area of knowledge to enable one of ordinary skill in the art at the time of the invention to practice the

invention without undue experimentation. However, as it will be discussed below this undue experimentation has not been overcame by the as filed application. At the time of the invention by the Applicant, the Art generally recognizes the regenerative capacities in multiple organ sytems of the small-intestinal submucosa (SIS) collagen-based material that is derived from the submucosa layer of porcine small intestine (Kropp PB, World J Urol. 1988; 16:262-7). Specifially, Ragheb et al., (US 6,774,278), teaches a coated implantable or injectable medical device (catheter, cannula, implant, column 6, last paragraph). The coating layer is designed to provide for enhancing the controlled delivery of a bioactive agent (column 3, paragraph 2). A bioabsorbable polymer such as a collagen-based polymer can be used as the coating biomaterial for minimizing irritation to the vessel wall (column 11, paragraph 2 and bridging column 12). The device may include two or more layers of different bioactive materials, with generally distinct bioactive function (column 13, paragraph 2). These bioactive layers do not have to be separated by a porous layer, but can instead lie directly against one another (column 15, paragraph 4). With regard to the use of another coated layer of radiopaque coating, Ragheb teaches that a conventional radiopaque coating preferably should be applied to the surface of the biomaterial based structure attached to a medical device, wherein the structure is employed for delivery of a bioactive agent (column 7, paragraph 6). Further, studies on stability of bioactive coating layers have provide insight into formation of complexes wherein different methods are used for binding of bioactive materials. For example, heparin can be attached to a variety of surfaces by complex formation with quaternary salts (Falb et al., 1969, Abstract), and by precipitation with amine, further stabilized by treatment with glutardialdehyde (Larsson RL et

al., 1977, p. 262). Hence, methods for controlling the bonding of biomaterials to create multiple layers are dictated by the most effective need to control the release of the bioactive material.

The application only provides a statement about the intended use of collagenous biomaterial 10, which comprises a submucosa layer, in individual or multi-layer devices. The term "bonded" as the physical deposition of collagenous layers claimed in the instant invention, encompasses the meaning of "to cause to adhere firmly" (Webster's Seven New Collegiate Dictionary). Thus, to make and use the claimed invention, a mere statement or sketch of the collagenous layer segments that are bonded to one another by means of using sutures, staples, and biocompatible adhesives such as collagen binding paste or dehydrating overlapping structures (p. 21, lines 16-24) is not reasonably predictable for any type of bonded collagenous multi-layers for making and using the genus as claimed. What is required is the knowledge in the prior art and/or description as to availability of a representative number of species of a bonded multilayer of bioabsorbable collagenous biomaterial that to could reasonably predict the nature of any other bonded collagenous multi-layer specie.

As such, and to the extent that the claimed invention is drawn to the make and use of any bioabsorbable collagenous biomaterial including multiple collagenous layer segments that are bonded to one another to promote remodeling of tissue of the patient at a site at which said collagenous biomaterial is implanted, the application doe not provide sufficient guidance and/or working examples for a skilled artisan to reasonably enable the claimed invention.

Due to the large quantity of experimentation necessary to generate the infinite number of derivative as recite in claims 54-60 and subsequent screening for promotion of remodeling of tissue of the patient at a site at which said collagenous biomaterial is implanted, one skilled in the

Art will have to perform extensive experimentation with each of these parameters to find the embodiments embraced by Applicant' claims, and as such, this experimentation would be considered undue.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 36-45, 53 are rejected under 35 U.S.C.103(a) as being unpatentable over Voytik-Harbin et al., (US Patent No. 6,444,229, filing date 01/27/2003) in view of Stinson (US 2004/0111149 A1).

Voytik-Harbin teaches an injectable collagenous biomaterial based gel composition comprising a vertebrate tissue submucosa derived from vertebrate such as a porcine derived small intestine submucosa (SIS, col. 2 paragraph 2; col. 4, paragraph 2), and a biological or known pharmacological agent for facilitating or inhibiting cellular proliferation dispersed therein (col. 11, paragraph 2). Additionally, the gellable composition can be prepared by grinding vertebrate submucosa into a powder and partially digesting it (col. 9, paragraph 2). Voytik-Harbin teaches that "the shape retaining gels of the present invention are translucent, having optical density ranging form about 0.1 to about 2.0 at A405 nm" (col. 8, paragraph 3) and that "additional components can be added to the hydrolysate composition before gellation of the composition at an injection site. For example, proteins, carbohydrates, growing factors, bioactive agents, nucleic acids or pharmaceutical can be added" (col. 8, paragraph 3). Further, with regard to the shape of the gel composition, Voytik-Harbin anticipates " in one embodiment the gel is formed to match the shape of an implantation site in a host" (col. 10, paragraph 2). The ability of sumbmucosal tissue-derived gel to serve as a cell culture scaffold was demonstrate by the ability of the four types of cells studied to attach, survive, proliferate and differentiae in vivo and *in vitro* (col. 16, paragraph 3). Voytik-Harbin teaches the type of implantable biomaterial formulation embrace by the instant application, for example, formulations including an injectable form (col. 10, paragraph 2).

Voytik-Harbin does not each that a radiopaque powder material such as tantalum or barium is mixed with implantable collagenous biomaterial.

However, at the time the invention was made, Stinson teaches that there is a need for bioabsorbable radiopaque markers for use on an implantable biomaterial such as an

endoprosthesis in order to improve radiopacity and the locality of an endoprosthesis during various medical procedures, and that one or more bioabsorbable radiopaque markers may be used on the implantable endoprostesis having little or no radiopacity (p. 1, paragraphs 0009, 0010; more specifically, p.2, paragraph 0023). Stinson teaches "in order to make an implant more radiopaque, a substance with absorbs more x-rays can be deposited on or mixed in with the implanted material". As such, with regard to the limitations as cited in claims 45, and 53, the radiopaque material is also received on the surface of an implantable biomaterial due to the mixing. Further, Stinson discloses that such radiopaque constituents (e.g., barium, tatalum) may be used as organic or metal radiopaque powders (p.7, paragraph 0073).

It would have been obvious then for one of ordinary skill in the art as a matter of design choice to construct the biomaterial in any shape know in the prior art such as the spherical form so long as the shape of the biocompatible material is compatible with an instrument used in the medical art of grafting for assisting with the placement of the biomaterial within the body of a grafted subject, particularly since shaping or molding techniques including sutures, staples, biocompatible adhesives are well-known in the prior art of record, as also exemplified by the primary reference.

Thus, the claimed invention was *prima facie* obvious.

Claims 45-53 are rejected under 35 U.S.C.103(a) as being unpatentable over any of Kropp (Urology, 1995), Whitson, US Pat No. 5997575, and Bonadio (US Patent No. 5,942,496), each of which in view of Stinson (US 2004/0111149 A1).

Kropp et al., Whitson et al. and Bonadio et al., all teach an implantable collagenous biomaterial comprising porcine derived small intestine submucosa (SIS), and a biological or known pharmacological agent dispersed therein (Kropp, entire document; Whitson, entire document; Bonadio column 30, last paragraph). Regarding the type of formulation including gel-like formulation, and membrane-type formulation, powdery formulation, they are all taught by the cited references (Kropp and Whitson teach membrane-type, and gel-like, injectable, dry, solid formulations, and Bonadio teaches powder formulations). While each of the cited references teaches a least one of the shapes cited in the elected species of the claimed invention, it would have been obvious for one of ordinary skill in the art as a matter of design of choice to construct the biomaterial in any shape known in the prior art so long as the shape of the biocompatible material is compatible with an instrument used in the medical art of grafting for assisting with the placement of the biomaterial within the body of a grafted subject, particularly since shaping or molding techniques including sutures, staples, biocompatible adhesives are well-known in the prior art of record.

Kropp et al., Whitson et al., and Bonadio et al., do not teach an incorporation of a radiopaque marker including barium, tatalum powder or bismuth on the surface of a collagenous material or SIS.

However, at the time the invention was made, Stinson teaches that there is a need for bioabsorbable radiopaque markers for use on an implantable biomaterial such as an endoprosthesis in order to improve radiopacity and the localtablity of an endoprosthesis during various medical procedures, and that one or more bioabsorbable radiopaque markers may be used on the implantable endoprosthesis having little or no radiopacity (p. 1 paragraphs 0009,

0010; more specifically p.2 paragraph 0023). Stinson teaches "in order to make an implant more radiopaque, a substance with absorbs more x-rays can be deposited on or mixed in with the implate material". As such, with regard to the limitations as cited in claims 45, and 53, the radiopaque material is also received on the surface of an implantable biomaterial due to the mixing. Further, Stinson discloses that such radiopaque constituents (e.g., barium, tatalum) may be used as organic or metal radiopaque powders (p. 7, paragraph 0073).

It would have been obvious then for one of ordinary skill in the art to incorporate any radiopaque powder material known in the prior art including barium, tantalum powder, and bismuth on the surface of the collagenous based biomaterial or SIS of each of the primary references. One of ordinary skill in the art would have been motivated to deposit or mix a radiopaque powder on the surface of or of within the implantable biomaterial made of a collagenous based tissue submucosa because Stinson teaches that there is a need for bioabsorbable radiopaque markers for use on implantable biomaterial such as an endoprosthesis in order to improve radiopacity and the locality of an endoprosthesis during various medical procedures, and that one or more bioabsorbable-radiopaque markers may be used on the implantable endoprosthesis having little or no radiopacity.

Thus, the claimed invention was *prima facie* obvious.

Claims 45-53 are rejected under 35 U.S.C.103(a) as being unpatentable over any of any of Badylak et al., (WO 96/24661), Badylak 2 (WO 96/25179), Cook et al., (WO 98/22158), Fearnot (US 6,358,284), Badylak 3 (US 2004/0078076), each of which in view of Stinson (US 2004/0111149 A1).

Badylak et al., Badylak 2, Cook et al., Fearnot, and Badylak 3 all disclose an implantable collagenous biomaterial comprising a tissue submucosa from at least one digestive submucosa and a biological or pharmacological agent dispersed therein (Badylak et al., entire document, specially, pages 5-8; Badylak 2, entire document, pages 5-8; Cook et al., entire document, specially pages 8-10; Fearnot, columns 2, 3, 6,7,18). Regarding the types of formulation of the implantable biomaterial, for example, as a comminuted amount or injectable form as recited in claims 43 and 53, respectively, they are all taugh by the cited references and are well known in the prior art of record (e.g., pages 15-21 of Cook et al., and Badylak 2, page 9). Each of the cited references also teach at least one of the shapes of the claimed invention, and to the extend that a least one of the cited shapes is not described in each of the cited references, it would have been obvious for one of ordinary skill in the art as a mater of design of choice to construct the biomaterial in any shape known in the prior art so long as the shape of the biocompatible material is compatible with an instrument used in the medical art of grafting for assisting with the placement of the biomaterial within the body of a grafted subject, particularly since shaping or molding techniques including sutures, staples, biocompatible adhesives are well-known in the prior art of record. Badylak et al., Badylak. 2, and Cook et al., all teach sterilization techniques to ensure that the tissue submucosa used for grafting are sterilized and free of bacterial contaminants, e.g., Badylak et al., pages 8, 19, 20, 32 and 33; Badylak. 2, pages 10-11; Cook et al., pages 10-15, Fearnot claims on column 18, Badylak 3). Absent evidence to the contrary, and as evidenced by the disclosure of Fearnot and Badylak 3, the tissue submucosa based biomaterials as prepared in Badylak et al., Badylak 2. and Cook et al., have all of the functional properties cited in the claims.

The primary references do not teach an incorporation of a radiopaque marker barium, tantalum powder, and bismuth on the surface of an implantable collagenous material or SIS. However, at the time the invention was made, Stinson teaches that there is a need for bioabsorbable radiopaque markers for use on an implantable biomaterial such as an endoprostesis in order to improve radiopacity and the localtablity of anendoprotesis during various medical procedures, and that one or more bioabsorbable radiopaque markers may be used on the implantable endoprosthesis having little or no radiopacity (p. 1 paragraphs 0009, 0010; more specifically p.2 paragraph 0023). Stinson teaches that "in order to make an implat more radiopaque, a substance with absorbs more x-rays can be deposited on or mixed in with the implanted material". As such, with regard to the limitations as cited in claims 45, and 53, the radiopaque material is also received on the surface of an implantable biomaterial due to the mixing. Further, Stinson discloses that such radiopaque constituents (e.g., barium, tatalum) may be used as organic or metal radiopaque powders (p. 7, paragraph 0073).

It would have been obvious then for one of ordinary skill in the art to incorporate any radiopaque power material known in the prior art including barium, tantalum, powder, and bismuth on the surface of the collagenous based biomaterial or SIS of each of the primary references. One of ordinary skill in the art would have been motivated to deposit a radiopaque powder material on the surface of or mix within the implantable biomaterial made of a collagenous based tissue submucosa because Stinson teaches that there is a need for bioabsorbable radiopaque markers for use on implantable biomaterial such as an endoprosthesis in order to improve radiopacity and the locality of an endoprosthesis during various medical

procedures, and that one or more biabsorbable-radiopaque markers may be used on the implantable endoprosthesis having little or no radiopacity.

Thus, the claimed invention was *prima facie* obvious.

Response to Arguments

Applicant's arguments of September 30, 2005 have been fully considered but are not found persuasive.

On page 2 of Applicant Arguments or Remarks made in the Amendment of September 30, 2005, Applicant argues that the amendment made to claim 54 in the final office action filed on March 28, 2005, has rendered the rejection of claim 54 mooted. Claim 54 has been amended to specify that the multi-layer bioabsorbable collagenous material includes "multiple collagenous layer segments that are bonded to one another".

Such is not persuasive. Claim 54 introduces new limitations that are not fully supported by Applicant's disclosure to make the invention reasonably predictable, given the state of the art at the time of filing that such collagenous material includes "multiple collagenous layer segments that are bonded to one another", as discussed above. Thus, claim 54 and its dependent claims 55-60 are not supported by the specification from the standpoint of enablement.

Applicant argues that amended claim 36 by including the term " a radiopaque marker component consisting *essentially of* a radiopaque powder material " has moved the claim away from Stinson disclosure.

Such is not persuasive. The following is a quotation from MPEP 2111.03:

[R-2] The transitional phrase "consisting essentially of" limits the scope of a claim to the specified materials or steps "and those that do not materially affect the basic and novel characteristic(s)" of the claimed invention.

In other words, Applicant has to demonstrate that in the radiopaque makers taught by Stinson's reference, incorporation of a radiopaque power substance into a bioabsorbable polymer material would materially affect the basic and novel characteristic of the claimed invention (i.e., a radiopaque power material). Stinson invention embraces the use of a micronized radiopaque powder (e.g. tantalum) to obtain appropriate radiopacity; incorporation of the drug into the polymer has the advantage of enhancing delivering of the drug (see, Paragraph 170, US 20040111149 A1).

On page 3 of Applicant Arguments or Remarks made in the Amendment of September 30, 2005, Applicant argues that amended claim 45 further adds the limitation of "the power particles of said radiopaque powder substance are in contact with the surface of the bioabsorbable collagenous material" adding that the Stinson invention doesn't teach a feature.

Such is not persuasive. Claim 45 includes the transitional phrase "consisting essentially of", as discussed above, Applicant fails to demonstrate that in Stinson's reference the surface of the biodegradable filaments is not in contact with the radiopaque powder (see, Paragraph 94).

Applicant argues that at pages 10 and 12 of the most recent Office Action, the Stinson references relied upon the teachings of a radiopaque marker that is distinct from the teachings of newly amended claim 45 and thus dependent claims 46-53.

Such is not persuasive, Applicants fails to provide specific direction or guidance to the manner from which the Stinson reference teaches away.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maria Leavitt whose telephone number is 571-272-1085. The examiner can normally be reached on M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Nguyen Dave can be reached on 571-272-0731. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

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